REMARKS

Claims 1-6, 8-16, 18-25, 27, and 28 are pending in this application. Claims 1-4, 8-11, 16, 18-21, 27, and 28 were variously rejected under 35 U.S.C. § 102. Claims 10-13, 16-23, 27, and 28 were rejected under 35 U.S.C. § 103. Claims 5, 6, 14, 15, 24, and 25 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

By this amendment, claims 18 and 27 have been canceled, claims 1, 10, and 20 have been amended without prejudice or disclaimer of any previously claimed subject matter. Support for the amendments can be found, *inter alia*, throughout the specification, for example, at page 37, lines 13-14, and in Example 2 at pages 44-47.

The amendments are made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. With respect to all amendments and cancelled claims, Applicant has not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicant expressly reserves the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Applicant has carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Rejections under 35 U.S.C. §102

Claims 1, 2, 8-11, 16, 18-21, 27, and 28 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Hutcherson, *et al.* (U.S. Pat. No. 5,663,153; "Hutcherson"). Claims 1-4 and 9 were rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Wagner, *et al.* (U.S. PG Pub. No. 2004/0030118; "Wagner"). Applicant respectfully traverses these rejections.

The claimed invention is directed to methods of preventing a symptom, reducing severity, and reducing recurrence of a symptom of herpes simplex virus infection in a human comprising administering an ISS-containing polynucleotide composition in the absence of administration of a herpes simplex virus antigen. Claim 1 is directed a method for preventing a symptom of herpes simplex virus infection through administration of the claimed ISS-containing polynucleotide to an individual exposed to herpes simplex virus, the administration prior to three days after virus exposure. Claims 10 and 20, respectively, are directed to reducing severity and reducing recurrence of a symptom of herpes simplex virus infection through parenteral administration of the claimed ISS-containing polynucleotide to the infected individual.

In order to anticipate, a reference must teach each and every element of a claimed invention. As outlined below, Applicant respectfully submits that neither of the cited references anticipates the claimed invention.

Hutcherson

Hutcherson describes administration of an oligonucleotide to selected cells or tissues to stimulate a local immune response by the cells or tissues and includes among the selected cells or tissues those that are infected with herpes simplex virus (HSV). The oligonucleotide administered in Hutcherson has at least one phosphorothioate bond. Hutcherson does not explicitly describe administration of an ISS-containing oligonucleotide for treating HSV infection, although the oligonucleotide administered to reduce the severity of HSV-induced stromal keratitis inherently contains a 5'-CG-3' dinucleotide (SEQ ID NO:2).

The Examiner admits that Hutcherson does not explicitly teach administration of the oligonucleotide prior to 3 days after HSV exposure. At page 3 of the Office Action, the Examiner asserts that the "broadest reasonable interpretation of this limitation includes administration of the CpG at any point prior to three days after virus exposure and is therefore anticipated by the teaching of prophylactic exposure in Hutcherson." Applicant respectfully disagrees with this assertion.

Administration of the oligonucleotide prior to 3 days after HSV exposure is not inherently taught in Hutcherson. In the discussion of treating HSV in which an oligonucleotide containing 5'-CG-3' was used, Hutcherson provides no definitive information on when the treatments took place relative to infection and clearly does not teach that administration occurs prior to 3 days after HSV exposure.[1] Hutcherson's statement in col. 10 that "[t]reatment with ISIS 1082 reduced stromal disease and vascularization on days 11, 13, and 15 post-infection" does not clarify this question. The statement either implies that the oligonucleotide was administered on days 11, 13, and 15 post-infection or that the disease in reduced on those days. In any event, this disclosure does not teach that the oligonucleotide is administered prior to 3 day after HSV exposure. The only other disclosure of administration of an oligonucleotide which inherently contains 5'-CG-3' is one injected into a wart, which is clearly more than 3 days after virus exposure.[2]

Further, Hutcherson does not describe a prophylactic treatment for HSV with an oligonucleotide containing a 5'-CG-3' sequence.

In the discussion of treating HSV with an oligonucleotide (which inherently contains 5'-CG-3'), Hutcherson describes only topical or local administration of the oligonucleotide to the site of infection. Hutcherson does not teach parenteral administration of an ISS-containing oligonucleotide for reducing severity and reducing recurrence of a symptom of HSV infection.

Accordingly, Applicant respectfully submits that Hutcherson does not anticipate the claimed invention.

Wagner

Wagner is directed to stimulation of an antigen-specific immune response by administration of CpG oligonucleotides prior to antigen exposure.[3] In support of this rejection, the Examiner asserts that "the broadest reasonable interpretation of claim 1 includes administration of the CpG at any point prior to three days after virus exposure, including prior to virus exposure in

[1] See Hutcherson, col. 10, lines 26-49.
[2] See, Hutcherson, col. 12, lines 4-6, and Example 11.
[3] See, for example, Wagner, paragraphs [0021], [0075], [0076], and [0077].

accordance with the teachings of Wagner *et al.*" Office Action, page 4. Applicant respectfully disagrees with this assertion.

Claim 1 is directed to administration of an ISS-containing oligonucleotide to an individual who has been exposed to herpes simplex virus (HSV). This feature has been emphasized by the amendment made herein. Wagner describes administration of CpG oligonucleotides before exposure to an antigen in order to "prepare for exposure to an antigen."[4]

Accordingly, Applicant respectfully submits that Wagner does not anticipate the claimed invention.

In sum, Applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. §102.

Rejections under 35 U.S.C. §103

Claims 10-13, 16-23, 27, and 28 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Wagner in view of Hutcherson. Applicant respectfully traverses this rejection and, as presented below, respectfully submits that a *prima facie* case of obviousness has not been established.

Claims 10 and 20, respectively, are directed to reducing severity and reducing recurrence of a symptom of herpes simplex virus infection through parenteral administration of the claimed ISS-containing polynucleotide to the infected individual. Thus, the composition is administered to an individual already infected with HSV.

As discussed above, Wagner is directed to stimulation of an antigen-specific immune response by administration of CpG oligonucleotides prior to antigen exposure. Wagner describes that the methods are useful for treating infectious diseases and includes HSV among the list of

[4] See Wagner paragraph [0077].

infectious viruses.[5] Thus, Wagner provides a method for treating HSV infection in an individual by systemic administration of the oligonucleotide before virus exposure.

Hutcherson describes treating an individual infected with HSV by local administration of an oligonucleotide containing at least one phosphorothioate bond.

The Examiner states that it would have been obvious to "modify the teachings Wagner *et al.* to include administration of the therapeutic oligonucleotide to an individual infected with herpes simplex virus according to the method of Hutcherson *et al.*" Office Action, page 6.

Wagner is directed to immune system remodeling based on stimulating cells with a CpG oligonucleotide before the cells encounter antigen. Modifying Wagner by administration of the oligonucleotide to an individual already infected with the virus as taught by Hutcherson would be to change the principle of operation of Wagner.

If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. M.P.E.P. §2143.01. One of skill in the art would have no motivation to combine the references or to modify the teachings of Wagner with those of Hutcherson.

Thus, Applicant respectfully submits that a prima facie case of obviousness has not been established.

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. §103.

[5] See, for example, Wagner, paragraphs [0082] and [0083].

CONCLUSION

Applicant believes that all issues raised in the Office Action have been properly addressed in this response. Accordingly, reconsideration and allowance of the pending claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, the Examiner is encouraged to contact Applicant's representative at the telephone number below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 377882001100.

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Respectfully submitted,

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